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Pertussis vaccination in patients with respiratory illness

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About the Experts

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Abbreviations used in this review

COPD = chronic obstructive pulmonary disease

DTaP-IPV = diphtheria, tetanus and acellular pertussis and inactivated polio vaccine

DTaP-IPV-HepB/Hib = diphtheria, tetanus and acellular pertussis and inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine

Tdap = adult tetanus, diphtheria and acellular pertussis vaccine

WHO = World Health Organization

This publication is intended as an educational resource for healthcare professionals. It discusses pertussis (whooping cough) infection in individuals with respiratory illnesses such as asthma and COPD, and outlines the prevention of this disease via immunisation with pertussis-containing vaccines. Vaccination against pertussis is fully-funded for children and some at-risk individuals in New Zealand as part of the National Immunisation Schedule.[1] The eligibility criteria for immunisation against pertussis in New Zealand has expanded. Pharmac has announced that as of 1 July 2020 the diphtheria, tetanus and pertussis (Tdap) vaccine Boostrix will replace the adult diphtheria and tetanus vaccine (ADT™ Booster) with the current eligibility criteria for Boostrix widened to include eligibility criteria currently in place for the ADT™ Booster vaccine.[2] There will be a restriction in place that tetanus booster at age 45 is given only to individuals who have not received four tetanus vaccinations in their lifetime.

Introduction

Pertussis is a highly contagious, potentially fatal, notifiable, respiratory disease caused by infection with *Bordetella pertussis* bacterium.[3] It is preventable through vaccination. One infected individual can pass pertussis on to up to 17 unprotected others, with a reproductive number (R_0) of 15-17.[4,5] Global estimates from WHO indicate approximately 16 million cases and 200,000 deaths from pertussis annually.[6] Regular pertussis epidemics and increasing burden of disease are evident in high-income countries such as New Zealand and Australia, despite high and stable vaccination rates.[7,8] New Zealand experiences a pertussis epidemic every 3-5 years, with several thousand cases reported during each cycle.[3] During the most recent national pertussis outbreak in New Zealand (Oct 2017 to May 2019) there were 2939 confirmed, 1636 probable and 122 suspected cases of pertussis.[9]

After entering the airways, the bacterium attaches to the cilia of respiratory epithelial cells and produces toxins that locally paralyse cilia and cause inflammation of the respiratory tract, interfering with the clearing of pulmonary secretions.[10] *B. pertussis* also has systemic effects on the immune system and can enter certain cells of respiratory origin such as epithelial cells and alveolar macrophages.[10,11]

Pertussis is characterised by violent attacks of spasmodic cough, sometimes with associated vomiting, lasting for up to 3 months.[3,8,12] Affected individuals may exhibit respiratory, nutritional and neurological (acute pertussis encephalopathy) complications.[3,8,11-13] In severe cases, extreme lymphocytosis can result in intractable pulmonary hypertension, respiratory failure and death.[14] In children, pertussis initially presents as a catarrhal phase with mild fever, runny nose and cough appearing 7-10 days after infection, gradually progressing to the paroxysmal phase with the distinct 'whooping cough', and then to the convalescent phase which may last for several months. Infants are less likely to exhibit the inspiratory 'whoop' and are more likely to present with gagging, apnoea, gasping, cyanosis, poor feeding or seizures.[15] The presentation and course of pertussis tends to differ in adults, without the classical symptoms, often with just a protracted cough of lesser severity in historically vaccinated individuals.[11] Typical complications of pertussis in adolescence and adulthood include otitis media, sinusitis, urinary incontinence, pneumonia, rib fracture, weight loss, and fainting.[11]

Despite effective immunisation programmes for infants and children, pertussis is re-emerging world-wide, with increasing incidence in those aged over 65 and in individuals with comorbidities such as asthma and COPD.[7,9,11,16] This increasing incidence is thought to be largely due to the waning of immunity over time in both vaccinated and non-vaccinated individuals with a history of *B. pertussis* infection.[11,17] Infected adolescents and adults act as reservoir for cyclic outbreaks of disease and are the major source of transmission of pertussis to partially immunised infants and children (**Figure 1**). In an aim to counteract this threat, some Western countries, including New Zealand, have implemented booster vaccine programmes for pregnant women and those in contact with at-risk newborns, while other countries have implemented general 10-year pertussis booster vaccination programmes.[1,11]

According to the latest figures from the Institute of Environmental Science and Research, over half (51%) of the 2110 whooping cough cases recorded in New Zealand over the past 12 months were adults aged ≥20 years; this age group represents 45% of hospitalisations.[9] The increasing incidence of pertussis among older children, adolescents and adults, especially those who are >65 years of age or with comorbidities and pathological conditions such as COPD and asthma is of particular concern and there is an unmet need of pertussis prevention in such groups both here and overseas.[11]

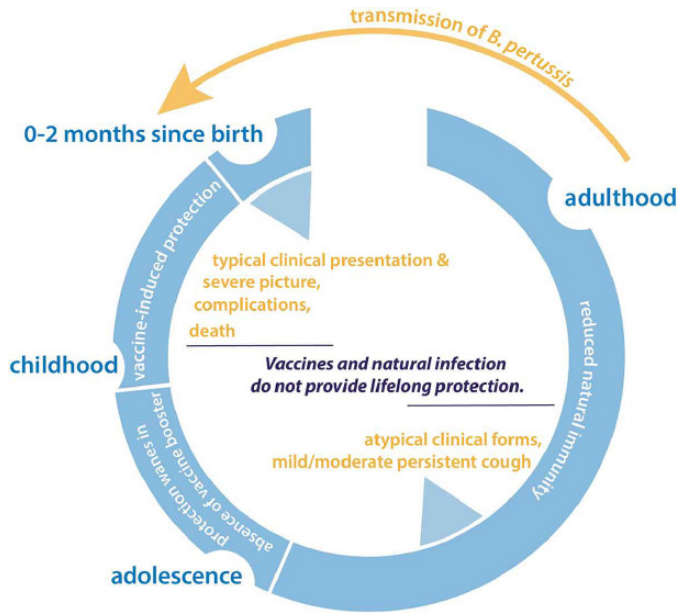

Figure 1. The pertussis cycle. In adulthood, the reduction of natural immunity not only renders individuals susceptible to infection with *B. pertussis*, but also makes them reservoirs of *B. pertussis*, who can transmit the infection to the unvaccinated population.[11]

Susceptibility and burden of pertussis in respiratory compromised individuals

Susceptibility to pertussis

Individuals with asthma and COPD are at an increased risk of complications associated *B. pertussis* and they appear to have a higher risk of contracting the infection.[18-20] Individuals with COPD and asthma are known to have a susceptibility to bacterial and viral infections and this could be due partly to pathologic changes in their airways leading to decreased barrier function and to immunosuppression from long-term corticosteroids.[11,18] Analysis of a large retrospective US claims database has revealed relative risks (RRs) of pertussis in individuals with COPD or asthma of 2.533 (95% CI 2.396-2.678) and 3.959 (95% CI 3.808-4.115), respectively, compared with those without COPD or asthma; in both COPD and asthma suffers the RR of pertussis was highest in patients aged 19-64 years (RRs 3.588 and 4.060, respectively).[20] In another US study, children with asthma exhibited a 1.92-fold increased risk of contracting pertussis, while adults with asthma exhibited a 1.14-fold increased risk.[18] An Australian study revealed an RR for pertussis of 1.64 (95% CI 1.06-2.55) in those with versus without asthma.[12]

Burden of disease

The burden of pertussis in the adult population is thought to be widely underestimated.[16,20] The burden increases with age, with asthma, with COPD and with smoking.[16,20] In fact, pertussis causes significant morbidity and mortality in children and adults with underlying respiratory illnesses with both asthma and COPD exacerbated by pertussis.[3,13,17,20,21]

In a Canadian case series involving 664 adolescents and adults with pertussis, increasing age raised the risk of pneumonia, fainting, urinary incontinence and hospitalisation, and both smoking and asthma significantly increased the mean duration of paroxysmal cough (5 vs 4 weeks and 5 vs 4 weeks), the risk of sinusitis (19 vs 11% and 16 vs 12%), and the number of nights disturbed by the illness (25 vs 20 nights and 26 vs 20 nights), respectively.[16] That study also revealed that 93% of patients had to increase their bronchodilator use as a result of pertussis. Consistent with these findings, a Finnish study found that *B. pertussis* infection resulted in lower FEV1/FVC (77.1% vs 80.7%, p=0.012) and more asthma symptoms.[22]

A number of international studies have also shown that the risk of hospitalisation after pertussis diagnosis is higher in patients with COPD and asthma, including a US study where 43.5% of hospitalised adolescents aged 12–20 years had a history of asthma and 26.8% of hospitalised adults aged ≥65 years had a history of COPD.[11,20,23] Consistent with these findings, a large Australian study involving adults aged ≥45 years found a 3.52-fold increased risk of hospitalisation for pertussis in individuals with versus without asthma.[19]

Individuals with COPD and asthma also exhibit a higher economic burden associated with pertussis than those without.[20] In a US study, compared with matched patients, patients with pertussis and pre-existing COPD or asthma accrued greater all-cause adjusted costs across study periods (US$3694 and US$1193 more, respectively, up to 45 days after infection, US$4173 and US$1301 more in the 3-months after infection; and US$6154 and US$1639 more in the 6-months after infection; all $p < 0.0001$).[20]

Vaccinating against pertussis

There are three pertussis-containing vaccines funded in New Zealand – INFANRIX-hexa, INFANRIX-IPV and Boostrix, and an unfunded vaccine (Adacel®).

INFANRIX-hexa, a combined diphtheria-tetanus-acellular pertussis, hepatitis B, enhanced inactivated polio and *Haemophilus influenzae type b* (DTaP-IPV-HepB/Hib) vaccine is indicated for primary and booster vaccination of infants and toddlers against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and *Haemophilus influenzae* type b.[24] The vaccine comes in a powder for suspension and is administered intramuscularly.

INFANRIX-IPV, a combined diphtheria-tetanus-acellular pertussis and enhanced inactivated polio suspension (DTPa-IPV) for intramuscular injection is indicated for active primary immunisation in infants from the age of 2 months against diphtheria, tetanus, pertussis, and poliomyelitis and as a booster dose for children up to 13 years of age who have previously been immunised with diphtheria, tetanus, pertussis (DTP) and polio antigens.[25]

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Boostrix, a combined diphtheria-tetanus-acellular pertussis (Tdap) suspension for intramuscular injection, is indicated for booster vaccination against diphtheria, tetanus and pertussis for individuals over 4 years of age.[26]

Adacel®, a combined acellular pertussis, diphtheria and tetanus vaccine suspension for intramuscular injection, is indicated for active immunisation against tetanus, diphtheria and pertussis in persons aged 10 years and over as a booster following primary immunisation. Adacel® may be administered during pregnancy for prevention of pertussis in young infants.[27]

In New Zealand, immunisation against pertussis is given free of charge as part of the National Immunisation Schedule to the following:[1,2]

- Infants and children at 6 weeks, 3 months, 5 months (DTaP-IPV-HepB/Hib [INFANRIX-hexa]), 4 years (DTaP-IPV [INFANRIX-IPV]) and 11 or 12 years of age (Tdap [Boostrix])
- Pregnant women during the second or third trimester of pregnancy (Boostrix)
- Unimmunised children up until their 18th birthday (Boostrix) – free of charge as part of a catch-up programme. Up to 4 doses are funded.
- Parents or primary caregivers of infants admitted to a Neonatal Intensive Care Unit or Specialist Care Baby Unit for more than 3 days (Boostrix)
- Individuals aged 45 years who have not had 4 previous tetanus doses (Boostrix)
- Individuals aged 65 years (Boostrix)
- Previously unimmunised or partially immunised individuals (Boostrix)
- Patients with tetanus-prone wounds (Boostrix)
- Patients post haematopoietic stem cell transplantation or chemotherapy, pre or post splenectomy, pre or post solid organ transplant, renal dialysis and other severely immunosuppressive regimens (Boostrix, INFANRIX-hexa and INFANRIX-IPV). Up to 4 doses are funded for (re-)vaccination.

Health professionals may recommend a whooping cough booster immunisation for adults who do not have a condition listed on the Schedule, but the vaccine will not be free*. Boostrix and Adacel® can be purchased for ineligible individuals.

There may also be merit in administering a second dose of pertussis booster vaccination after 10 years in adults as a proactive approach to staying well while aging, with a recent study demonstrating such administration immunogenic and well tolerated.[28]

* As of 1 July 2020, Boostrix has replaced the adult diphtheria and tetanus vaccine (ADT™ Booster) and the current eligibility criteria for Boostrix has been widened to include eligibility criteria currently in place for the ADT™ Booster vaccine.[2]

How safe is vaccination against pertussis?

The safety profile of acellular vaccines is well established and Tdap booster doses appear well tolerated in all age groups.[29] In a large study involving elderly individuals aged ≥65 years, the safety profile of Tdap was comparable to that in younger populations.

Common and rare responses to the three pertussis vaccines are as follows:[3]

Infanrix-IPV (DTaP-IPV) Infanrix-hexa (DTaP-IPV-HepB/Hib)	
Common Responses	• Mild pain, redness and swelling around injection site • Decreased appetite • Vomiting or diarrhoea • Irritability, restlessness • Unusual crying • Limb swelling
Rare Responses	• Hives • Temporary low platelet count • Persistent inconsolable screaming in infants • Hypotonic, hyporesponsive episode (HHE) in infants • Convulsion
Boostrix (Tdap)	
Common Responses	• Pain and swelling around the injection site may prevent normal everyday activities for 24–48 hours • Headache or nausea • Muscle or joint stiffness or pain
Rare Responses	• Hives • Sterile abscess at the injection site
Adacel (Tdap)	
Common Responses	• Pain and swelling around the injection site may prevent normal everyday activities for 24–48 hours • Headache or nausea • Muscle or joint stiffness or pain
Rare Responses	• Hives • Sterile abscess at the injection site • Brachial neuritis

As with any medicine, very rarely a severe allergic reaction (anaphylaxis) can occur following immunisation.

How long does pertussis immunity last?

While acellular pertussis vaccines (like those used in New Zealand) are less reactogenic than whole-cell pertussis vaccines, they also appear to be less enduring.[8,30] Studies investigating immune persistence after DTaP immunisation in children estimate the average duration of protection from DTaP to be 3-4 years, with only 10% of children protected against pertussis 8.5 years following the last dose.[30] In adolescents and adults, evidence suggests 10 years as an optimal interval for Tdap vaccine doses and a second Tdap booster has been found to be highly immunogenic and well tolerated in adults who have previously received one Tdap dose 10 years prior.[30]

EXPERTS' CONCLUDING REMARKS

This educational resource is becoming available while the world is awaiting a vaccine for the novel coronavirus, highlighting the public health benefits of vaccination. New Zealand has a comprehensive paediatric vaccination programme and life-threatening whooping cough is rare. However, the protection seems to wane after a decade and, in the context of recurrent outbreaks, previously vaccinated individuals are at risk of infection.

As adult respiratory physicians we see many patients with a postinfectious cough. During times of a cyclic endemic, we frequently confirm pertussis via serological testing as the underlying organism. Classically, by the time the serological test is positive, treatment with a macrolide antibiotic is of little benefit as this bacterium has been cleared, however, a cough which causes significant reduction in the quality of life through sleep disturbance, chest pain, rib fractures or vomiting often continues for about 3 months. The impact of pertussis is likely to be higher among patients with chronic respiratory disease.

Given the tolerable safety profile, the cyclic nature of the illness and the impact on quality of life, it seems prudent to discuss the opportunity of a revaccination for whooping cough with our patients, particularly our patients with chronic lung conditions. The change in the immunisation schedule, from 1 July 2020 should prompt us to actively consider vaccination for those who are eligible.

TAKE-HOME MESSAGES

- Pertussis is a highly contagious, potentially fatal, notifiable, respiratory disease
- One infected individual can pass pertussis on to up to 17 unprotected others
- NZ experiences a pertussis epidemic every 3-5 years, with several thousand cases reported during each cycle
- The impact of pertussis is likely to be higher among patients with chronic respiratory disease
- Pertussis is preventable through vaccination
- The change in the immunisation schedule from 1 July 2020 should prompt clinicians to actively consider pertussis vaccination for those who are eligible.

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